ABSTRACT

PEPTIDES WHOSE UPTAKE BY CELLS IS CONTROLLABLE

A generic structure for the peptides of the present invention includes **A – X – B - C**, where **C** is a cargo moiety, the **B** portion includes basic amino acids, **X** is a cleavable linker sequence, and the **A** portion includes acidic amino acids. The intact structure is not significantly taken up by cells; however, upon extracellular cleavage of **X**, the **B – C** portion is taken up, delivering the cargo to targeted cells. Cargo may be, for example, a contrast agent for diagnostic imaging, a chemotherapeutic drug, or a radiation-sensitizer for therapy. Cleavage of **X** allows separation of **A** from **B**, unmasking the normal ability of the basic amino acids in **B** to drag cargo **C** into cells near the cleavage event. **X** is cleaved extracellularly, preferably under physiological conditions. D-amino acids are preferred for the **A** and **B** portions, to minimize immunogenicity and nonspecific cleavage by background peptidases or proteases.